REMARKS/ARGUMENTS

Claims 1-3, 10, and 12-19 remain pending in this application, and are rejected. Claims 4-9, 11, and 20-39 have been withdrawn from consideration.

A. Restriction

In paragraphs 1-6 of the Office Action, the Examiner indicated that Claims 1-19 were drawn to a method of folding a polypeptide and that Claims 20-39 were drawn to a method of screening for an optimal folding environment for a denatured peptide. In paragraph 4, the Examiner further indicated that the osmolytes of Claims 4-11 were subject to a Markush group like restriction for examination purposes. Similarly, in paragraph 5, the Examiner indicated that Claim 19 contained a Markush group that was subject to restriction. Applicant understands that if no prior art is found that anticipates or renders obvious the elected species, the search of the Markush-type claims will be extended. See MPEP § 803.02.

Applicant confirms the election of Claims 1-19 and urea and glutathione to be examined with traverse. Applicant respectfully submits that Claims 1-19 and Claims 20-39 should not be subject to a restriction requirement. In this regard, Applicant notes that Claims 1-19 are directed to a method for folding a denatured polypeptide while Claims 20-39 are directed to a method for screening an optimal folding environment for a denatured polypeptide. Indeed, the Examiner indicates that both sets of claims are classified in Class 435, Subclass 4. Applicant believes that no serious burden would be imposed on the Examiner. See MPEP §803.01. As such, withdrawal of the restriction request is respectfully requested.

B. Drawings

In accordance with the Examiner's instructions in paragraph 7 of the Office Action, formal drawings will be filed once the application is allowed.

C. Information Disclosure Statement

Pursuant to Paragraph 8 of the Office Action, Applicant is submitting herewith an Information Disclosure Statement in accordance with the Examiner's instructions for his consideration. The IDS contains several references that were published after Applicant's priority date which are discussed below and are not "prior art." Applicant respectfully submits that the claims are patentable in view of the cited references.

D. Claim Rejections Under Section 112

In paragraph 10 of the Office Action, the Examiner rejected Claim 15 as being nonenabling to the extent that it claims "prevention" of the aggregation of unfolded proteins. In paragraph 12, the Examiner also rejected Claim 15 as being indefinite for using the word "substantially." Applicant has amended to recite in order to overcome the Examiner's rejections.

In paragraph 13, the Examiner rejected Claim 13 because "incapable of" does not equate to must not invariably occur and thus the claim is indefinite as indicating only a potential function/action. Applicant has amended the claim to recite the term "substantially." Applicant respectfully submits that this term is definite in view of the folding array data (Table 1).

E. Claim Rejections Under Section 102

1. Altamirano References

In paragraphs 16 and 17, the Examiner rejected Claims 1-3, 10, 13-15 as being anticipated under 35 U.S.C. § 102 by Altamirano (1997) or Altamirano (1999). Applicant respectfully traverses the rejection. Applicant notes that the claimed invention is directed to a method for refolding a denature polypeptide which includes both an osmolyte and a "chaperonin." This is not the same as the fragmented "minichaperone system" described in the

cited Altamirano references. As such, Applicant respectfully requests that the Examiner withdraw the rejection under Section 102.

The minichaperone system is inferior to and will not function with most commonly used polypeptides. In this regard, the Wang (1998) and Weber (1998) articles included in the Information Disclosure Statement show that the Altamirano minichaperone system fails to fold various stringent protein substrates. In cases where successful folding with the minichaperone is observed, Altamirano and his coworkers refolded one stringent class III chaperonin dependent protein, but only under conditions where rodanese can fold by itself (so-called "permissive" 25° C folding conditions). See Wang (1998); Smith & Fisher (1995). Thus, it does not appear that the minichaperone was even required to fold this protein to any degree.

In particular, Wang (1998) and Weber (1998) showed that the minichaperone system could not function to fold malate dehydrogenase. In contrast, as illustrated in Example 8, the present invention was capable of working with other substrates (such as malate dehydrogenase). See also (Tieman 2001). Further, subsequent work by the inventors (Voziyan 2000) indicates that the present invention involving chaperonin/osmolyte systems shows that it works with citrate synthase, another one of the test substrates that the minichaperones failed to fold. See Weber (1998). The primary difference between the claimed invention, which uses the oligomeric version of the chaperone, and that of the minichaperone fragment is that the latter cannot capture folding polypeptides or stabilize a metastable protein state for any length of time.

In short, there is nothing in the prior art that teaches the use of an osmolyte/"chaperonin" system to promote the folding of a polypeptide. Applicant respectfully submits that the Altamirano references do not teach or suggest the claimed invention. As such, withdrawal of the rejection is requested.

2. Gorovitz Reference

The Examiner next rejects Claims 1-3, 10 and 15-16 as being anticipated by Gorovitz (1997). Applicant respectfully traverses the rejection. Applicant notes that the claimed invention is directed to a method for refolding a denature polypeptide using a chaperonin and an osmolyte, "thereby promoting the folding of said polypeptide from its unfolded to its folded state." The Gorovitz article does not teach or suggest the claimed invention. As such, Applicant respectfully requests that the Examiner withdraw the rejection under Section 102.

The Gorovitz article illustrates that differing denaturing conditions (urea vs. thermal) change the chaperonin requirements (GroEL, GroES ATP vs. GroEL GroES ADP). The article simply created a different denatured protein to bind to the chaperonin. The folding of the protein DHFR was initiated in the presence of GroEL with residual urea present. However, the inclusion of urea did not in any way promote the folding of DHFR to its native conformation. DHFR easily folds by itself without the aid of chaperonins and as such, the urea did not promote the folding of the protein. Thus, Applicant respectfully submits that the claimed invention is not anticipated or rendered obvious by the claimed invention.

In view of the foregoing amendments and remarks, it is respectfully submitted that the claims are now in condition for allowance and eventual issuance. Such action is respectfully requested. Should the Examiner have any further questions or comments in order to obtain allowance, he is invited to contact the undersigned attorney at the number listed below.

Acknowledgement of receipt is respectfully requested.

Respectfully submitted,

By: _____

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